This marketing scheme is targeted to those patients in a "progressive[6]" form of MS, i.e. referred to sometimes as a "continuous exacerbation."

39. Questcor did these things in reckless disregard of the unusually serious safety profile for H.P. Acthar Gel, as reflected in its FDA-approved label. Questcor has attempted to conceal and cover-up its payment of kickbacks and its illegal promotion of H.P. Acthar Gel by making false statements to the FDA and directing employees to conceal evidence by failing to disclose, inter alia, the full nature and extent of its advertising, promotional and marketing materials and plan. Questcor's unlawful promotion of H.P. Acthar Gel has involved the unlawful making of false records or statements and/or causing false claims to be submitted for the purpose of getting the false records or statements to bring about the federal government's payment of a false or fraudulent claim. In addition to the above and as described more fully herein, Questcor managers routinely ignore or encourage illegal promotional activities, and they certainly do not investigate and correct such misconduct as their Corporate Compliance Program purports to require. These practices continued after the merger with Mallinckrodt.

40. Questcor's conduct has had a material effect on the Government Health Care Programs decision to pay for H.P. Acthar Gel. Had these programs known that

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[6] According to the FDA Approved Label, Acthar is only indicated for use for "acute" exacerbations. There are four classes of MS. Most patients have the form of relapsing-remitting MS. The other three types of MS are a "progressive" form, which means the patients are in a constant declining exacerbation. These three types of MS patients are not indicated for Acthar because they are not having acute relapses.

reimbursements were being made for H.P. Acthar Gel caused by Questcor's unlawful promotion, it would not have made such reimbursements. The above-described, and the specific details, facts and circumstances allege herein is referred to herein as the "Fraudulent Marketing Scheme." Questcor's perpetration of this Fraudulent Marketing Scheme is ongoing. These practices continued after the merger with Mallinckrodt.

VI. FEDERAL LAWS REGARDING REIMBURSEMENT AND FRAUD ENFORCEMENT

A. The Government Health Care Programs

41. The Medicare Program, Title XVIII of the Social Security Act, 42 U.S.C. §1395 et seq., (hereinafter "Medicare") is a Health Insurance Program administered by the Government of the United States that is funded by taxpayer revenue. The program is overseen by the United States Department of Health and Human Services. Medicare is a health insurance program that provides for the payment of prescription drugs, hospital services, medical services and durable medical equipment to persons over sixty-five (65) years of age and others that qualify under the terms and conditions of the Medicare Program.

42. The Medicaid Program, Title XIX of the Social Security Act, 42 U.S.C. § 1396-1396v (hereafter "Medicaid"), is a Health Insurance Program administered by the Government of the United States and the various individual States and is funded by State and Federal taxpayer revenue. The Medicaid Program is overseen by the United States Department of Health and Human Services. Medicaid was

designed to assist participating states in providing medical services, durable medical equipment and prescription drugs to financially needy individuals that qualify for Medicaid.

43. The Civilian Health and Medical Program of the Uniformed Services ("CHAMPUS") (now known as "TRICARE"), 10 U.S.C. secs. 1071-1106, provides benefits for health care services furnished by civilian providers, physicians, and suppliers to members of the Uniformed Services and to spouses and children of active duty, retired and deceased members. The program is administered by the Department of Defense and funded by the Federal Government. CHAMPUS pays for, among other items and services, prescription drugs for its beneficiaries.

44. The federal government, through its Departments of Defense and Veterans Affairs, Bureau of Prisons, Native and American Indian Health Services, and Public Health Service maintains and operates medical facilities including hospitals, and receives and uses federal funds to purchase prescription drugs for patients treated at such facilities and otherwise.

45. The Federal Employees Health Benefits Program ("FEHBP") provides health care benefits for qualified federal employees and their dependents. It pays for, among other items and services, prescription drugs for its beneficiaries. (Together these programs described above shall be referred to as "Federal Health Care Programs" or "Government Health Care Programs").

B. The False Claims Act

46. The Federal FCA, 31 U.S.C. § 3729(a)(1)(A)[7] makes "knowingly[8]" presenting or causing to be presented to the United States any false or fraudulent claim for payment, a violation of federal law for which the United States may recover three times the amount of the damages the government sustains and a civil monetary penalty of between $5,500 and $11,000 per claim for claims made on or after September on or after 29, 1999[9].

47. The Federal FCA, 31 U.S.C. § 3729(a)(1)(B) makes "knowingly" making, using, or causing to be used or made, a false record or statement to get a false or fraudulent claim paid or approved by the Government, a violation of federal law for which the United States may recover three times the amount of the damages the

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[7] On May 22, 2009, the Fraud Enforcement and Recovery Act (FERA) was enacted into law which, inter alia, amended the False Claims Act. Part of the amendment renumbered ceratin sections. Under FERA, effective 5/22/09 3729(a)(1) became 3729(a)(1)(A). Likewise, 3729(a)(2) became 3729(a)(1)(B) and 3729(a)(3) became 3729(a)(1)©. Since the allegations include a time period before and after 5/22/09, references are to be applicable sections

[8] "Knowingly" means the defendant (1) had actual knowledge that the claim is false; (2) acted with deliberate ignorance of the truth or falsity of the claims; or (3) acted with reckless disregard of the truth or false of the other claim. 31 U.S.C. § 3729(b)(1)(A)(1-3) and Section 2729(b)(1)(B).

[9] On November 2, 2015, President Obama signed into law the Federal Civil Penalties Inflation Adjustment Act Improvements Act of 2015 (the 2015 Act), which further amended the Federal Civil Penalties Inflation Adjustment Act of 1990. The 2015 Act updates the process by which federal agencies adjust applicable civil monetary penalties for inflation to retain the deterrent effect of those penalties. The 2015 Act requires that not later than July 1, 2016, and not later than January 15 of every year thereafter, the head of each agency must, by regulation published in the Federal Register, adjust each CMP within its jurisdiction by the inflation adjustment described in the 2015 Act. For violations of the False Claims Act, the interim final rule minimum per-claim CMP's will increase to $10,781 from $5,500, and maximum per-claim CMPs will jump to $21,563 from $11,000. The increase takes effect August 1, 2015 and applies to violations after November 2, 2015.

Government sustains and a civil monetary penalty of between $5,000 and $10,000 per claim ($5,500 and $11,000 for claims made on or after September 29, 1999).

48. The Federal FCA, 31 U.S.C. sec. 3729(a)(1)© makes any person, who conspires to defraud the United States by getting a false or fraudulent claim allowed or paid, liable for three times the amount of the damages the Government sustains and a civil monetary penalty of between $5,000 and $10,000 per claim ($5,500 and $11,000 for claims made on or after September 29, 1999).

49. The Federal FCA defines a "claim" to include any request or demand, whether under contract or otherwise, for money or property which is made to a contractor, grantee, or other recipient if the United States Government provides any portion of the money or property which is requested or demanded, or if the Government will reimburse such contractor, grantee, or other recipient for any portion of the money or property which is requested.

C. The Anti-Kickback Statute

50. The Medicare, Medicaid and Anti-Kickback Act ("AKA") 42 U.S.C. §1320a-7b(b), makes it illegal to:

> *offer,* receive, or solicit *any remuneration*, kickback, bribe, or rebate, whether directly or indirectly, overtly or covertly, in cash or in kind, to or from any person in order *to induce such person to purchase*, lease, or order, or to arrange for or recommend the purchasing, leasing, or ordering of *any good, service, or item for which payment may be made in whole or in part under a Federal Health Care Program.*

VII. BACKGROUND OF THE REGULATORY FRAMEWORK

A. The Food and Drug Administration ("FDA") Regulatory System

1. The FDA Regulates What Drugs May Be Marketed, and the Uses For Which They May Be Marketed.

51. Under the Food, Drug and Cosmetics Act ("FDCA"), 21 U.S.C. §§ 301-97, new pharmaceutical drugs cannot be marketed in the United States unless the sponsor of the drug demonstrates to the satisfaction of the FDA that the drug is safe and effective for each of its intended uses. 21 U.S.C. § 355(a), (d). Approval of the drug by the FDA is the final step in a multi-year process of study and testing.

52. To determine whether a drug is *"safe and effective,"* the FDA relies on information provided by a drug's manufacturer; it does not conduct any substantial analysis or studies itself. Applications for FDA approval (known as New Drug Applications or "NDAs") must include *"full reports of investigations which have been made to show whether or not such drug is safe for use and whether or not such drug is effective in use."* 21 U.S.C. § 355(b)(1)(A).

53. Under the nation's food and drug laws, a drug may not be introduced into interstate commerce unless its sponsor has shown that the drug is safe and effective for the intended conditions of use. *21 U.S.C. § 321.* The law requires that *"adequate and well controlled investigations"* be used to demonstrate a drug's safety and effectiveness. *21 U.S.C. § 355(d)(7).* The FDA approves a drug if there are *"adequate and well-controlled clinical trials"* that demonstrate a drug's safety and effectiveness for its *"intended conditions"* of use. *21 U.S.C. § 355(d)(5).* The

"intended conditions" for use of a drug are listed in the drug's labeling, which is reviewed and approved by the FDA. *21 U.S.C. § 355(d)(1) & (2).* Indications for use that are not listed in a drug's labeling have not been approved by the FDA. *37 Fed. Reg. 16,503 (1972).*

54. The standards that govern the FDA safety and effectiveness requirements are contained in statutes, regulations, notices and guidance documents. The statutory requirement that a drug's effectiveness be demonstrated by *"adequate and well-controlled clinical investigations"* has been interpreted to mean a clinical study with (1) clear objectives; (2) adequate design to permit a valid comparison with a control group; (3) adequate selection of study subjects; (4) adequate measures to minimize bias; and (5) well defined and reliable methods of assessing subjects' responses to treatment. *21 C.F.R. § 314.26.*

55. The FDA also requires the need for reproducibility and reliability of clinical data in the trials that support a drug's approval. In order to address this requirement, the FDA generally requires two pivotal, adequate and well-controlled trials to support approval, except in certain circumstances. As stated by the FDA in its 1998 Guidance to the Industry, *"it has been FDA's position that Congress generally intended to require at least two adequate and well controlled studies, each convincing on its own, to establish effectiveness."* *See U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Guidance for Industry: Providing Clinical Evidence o Effectiveness for*

Human Drugs and Biological Products, May 1998. See, e.g., Final Decision on Benylin, 44 FR 51512, 518 (Aug. 31, 1979).

56. FDA's position is based on the language in the statute and the legislative history of the 1962 amendments. Language in a Senate report suggested that the phrase *"adequate and well-controlled investigations"* was designed not only to describe the quality of the required data but also the *"quantum"* of required evidence. *See S. Rep. No. 1744, Part 2, 87thCong. 2d Sess. 6 (1962)*. Nevertheless, FDA has been flexible within the limits imposed by the Congressional scheme, broadly interpreting the statutory requirements to the extent possible where the data on a particular drug was convincing. In some cases, FDA has relied on pertinent information from other adequate and well-controlled studies of a drug, such as studies of other doses and regimens, of other dosage forms, in other stages of disease, in other populations, and of different end points, to support a single adequate and well-controlled study demonstrating effectiveness of a new use. In these cases, although there is only one study of the exact new use, there are, in fact, multiple studies supporting the new use, and expert judgment could conclude that the studies together represent substantial evidence of effectiveness.

57. In other cases, FDA has relied on only a single, adequate and well-controlled efficacy study to support approval - generally only in cases in which a single multi center study of excellent design provided highly reliable and statistically strong evidence of an important clinical benefit, such as an effect on survival, and a confirmatory study would have been difficult to conduct on ethical

grounds. In section 115(a) of the Modernization Act, Congress amended section 505(d) of the Act to make it clear that the Agency may consider *"data from one adequate and well-controlled clinical investigation and confirmatory evidence"* to constitute substantial evidence if FDA determines that such data and evidence are sufficient to establish effectiveness. In making this clarification, Congress confirmed FDA's interpretation of the statutory requirements for approval and acknowledged the Agency's position that there has been substantial progress in the science of drug development resulting in higher quality clinical trial data.

58. Cases in which the FDA has approved a drug on the basis of one clinical trial plus, confirmatory evidence are rare. They include instances of large, independently conducted multi center trials with strong empirical results, with internal consistency across multiple outcomes, such that "sponsors faced ethical boundaries" in conducting a second placebo-based trial. Clinical trials that are not controlled, blinded, randomized and whose endpoints are not prospectively and objectively determined and measured may be used in early stage drug development phases, but are exceptionally unlikely to qualify as *"adequate and well-controlled"* clinical trials needed to support FDA approval. After a drug is approved, the FDA continues to exercise control over the product labeling. To protect patients from safety concerns, the FDA may require a label change to reflect the increased risk of various side effects or interactions, restrict a drug's indications, or, in extreme cases, force a withdrawal from the market. *21 C.F.R. § 201.57(3).*

2. FDA Regulations Prohibit Off Label Marketing Through False and Misleading Statements About a Drug's Use

59. FDA regulations restrict how drug companies may market and promote approved drugs. *See 21 U.S.C. §§ 331, 352; 21 C.F.R. § 314.81.* Drug labels, including all marketing and promotional materials relating to the drug, may not describe intended uses for the drug that have not been approved by the FDA. *21 U.S.C. §§ 331, 352.* Illegal "misbranding" can result in criminal penalties. *21 U.S.C. § 333.*

60. Drug companies such as Defendant must submit specimens of mailing pieces and any other labeling or advertising devised or used for promotion of the drug product at the time of initial dissemination of the labeling and at the time of initial publication of the advertisement for a prescription drug product. Each submission is required to be accompanied by a completed transmittal Form FDA–2253. This constitutes a specific and material representation that all promotional items are being disclosed and provided to the FDA. Moreover, it constitutes an implied representation that the promotion and marketing that is being done through verbal communications, including inter alia, any drug company's speech or *"advertisement"* for the product, which are also subject to the prohibitions against off label marketing in 21 C.F.R. 202.1, is consistent and in line with any written communications being submitted to FDA.

61. The same general requirements about the promotion of prescription drugs apply to both professional and consumer-oriented marketing. In particular,

promotional materials may only make claims that are supported by *"substantial"* scientific evidence (according to strict scientific procedures) and they may not be false, deceptive or misleading. FDA oversight helps ensure a *"fair balance"* in all promotional claims and materials. Federal regulations require that the risks as well as the benefits be clearly identified and given appropriate prominence. Promotional materials must be consistent with the FDA-approved product labeling. This restriction pertains to the clinical indications for which the drug has been approved *as well as the dosing regimen that is supported by the clinical trials* that were undertaken to establish safety and efficacy.

62. A drug company that wishes to market or otherwise promote an approved drug for uses other than those listed on the approved label, must resubmit the drug for a series of clinical trials similar to those required for the initial FDA approval. *See Food and Drug Administration Modernization Act of 1997 ("FDMA"), 21 U.S.C. §§ 360aaa(b), ©; see also 21 C.F.R. § 314.54 (outlining the administrative procedure for filing an application for a new indication); 21 U.S.C. §§ 301 et seq.* A supplemental NDA must be filed. Unless and until an additional indication is approved by the FDA, the unapproved use is considered to be "off-label."

63. The term "off-label" refers to the use of an approved drug for any purpose, or in any manner, other than what is described in the drug's labeling. Off-label use includes treating a condition not indicated on the label, treating the indicated condition at a different dose or frequency than specified on the. label, or

treating a different patient population, e.g., treating a child when the drug is approved to treat adults.

64. Although the FDA is responsible for ensuring that a drug is safe and effective for the specific approved indication, the FDA does not regulate the practice of medicine. Once a drug is approved for a particular use, the FDA does not prohibit physicians from prescribing the drug for uses that are different than those approved by the FDA. When considering off-label prescribing, physicians depend on the patient-specific evidence they have available to them. This includes the particular patient, the severity of his or her problems, the successfulness of prior treatment, and the risks of not treating. Whether contemplating on- or off-label use, physicians also rely on personal experience, recommendations from colleagues and academics, educational seminars, and clinical trials evidence. Much of what physicians rely on is information (or, as the case may be, misinformation) provided by sales representatives from drug makers, drug company sponsored continuing medical education ("CM") courses and speaker programs, and drug company sponsored clinical trials.

65. Although physicians may prescribe drugs for off-label usage, the law prohibits drug manufacturers from marketing or promoting a drug for a use that the FDA has not approved, or for a patient group that is unapproved. Specifically, a manufacturer illegally "misbrands" a drug if the drug's labeling (which includes all marketing and promotional materials relating to the drug) describes intended uses for the drug that have not been approved by the FDA. *21 U.S.C. §§ 331, 352.* The

statute, *21 U.S.C. § 331(d)*, and its implementing regulations, and 21 C.F.R. 202.1(e)(4)(i)(a) prohibit any advertising that recommends or suggests an off-label use for an approved drug, and the FDA has interpreted "advertising" to include a significant amount of speech that would not typically be considered advertising. *See Final Guidance on Industry-Supported Scientific and Educational Activities, 62 Fed. Reg. 64,074 (Dec. 3, 1997).* The FDA *"interprets the term `advertisement' to include information (other than labeling) that originates from the same source as the product and that is intended to supplement or explain the product."*

66. Any drug company's speech explaining one of its products is an *"advertisement"* for the product and is subject to the prohibitions against off label marketing in 21 C.F.R. 202.1, as well as the FDA's *"fair balance"* requirement, described below. While a drug company may be entitled to certain First Amendment protection for truthful speech, see *U.S. v. Caronia*, 703 F.3d 149 (2d Cir.2012), off-label promotion that is false or misleading is not entitled to First Amendment protection. *Caronia,* at 166 n. 10. *See Cent. Hudson,* 447 U.S. at 566, 100 S. Ct. 2343. Under 21 U.S.C. § 331(a), a defendant may be prosecuted for untruthfully promoting the off-label use of an FDA-approved drug, *e.g.,* making false or misleading statements about a drug.

67. Section 202.1(e)(6)(xi) provides that an advertisement may not use *"literature, quotations, or references for the purpose of recommending or suggesting conditions of drug use that are not approved or permitted in the drug package labeling."* See also 21 U.S.C. § 331(d) (prohibiting distribution of a drug for

non-approved uses); id. § 331(a) (prohibiting distribution of a misbranded drug); id. § 360aaa (permitting dissemination of material on off-label uses only if the manufacturer meets certain stringent requirements).

68. The FDA regulations that fall under the general rubric of 21 C.F.R. 202.1(e)(6) et seq. ban advertisements that are false, lacking in fair balance, or otherwise misleading. Thus, the use of unsubstantiated comparative claims also is prohibited by law. 21 U.S.C. § 352; 21 C.F.R. § 202.1(e)(6). Thus, companies such as Questcor may not promote their approved drugs through unsubstantiated comparative claims that exalt their drugs as safer or more efficacious than competitor drugs. Such promotion renders a drug "misbranded" and no longer eligible for reimbursement by Government Programs, including Medicaid.

69. The regulations prohibit an advertisement that *"contains a representation or suggestion that a drug is safer than it has been demonstrated to be by substantial evidence or substantial clinical experience, by selective presentation of information from published articles or other references that report no side effects or minimal side effects with the drug or otherwise selects information from any source in a way that makes a drug appear to be safer than has been demonstrated." 21 C.F.R. 202.1(e)(6)(iv).*

70. The regulations require drug companies to present a "true statement" of information relating to the side effects, contraindications and effectiveness of the drug use. *21 C.F.R. 202.1(e)(5) et seq.* A company violates this regulation if it presents *"false or misleading"* information about a drug's side effects or does not

"fair[ly] balance" information relating to the safety and efficacy of the drug use against information about its side effects and contraindications. *Id.*

71. Section 202.1(1)(2) broadly describes *"labeling"* of a drug as including any material accompanying a drug product that is supplied and disseminated by the manufacturer, packer or distributor of the drug.

72. Section 201.56 requires labeling to be *"informative and accurate and neither promotional in tone nor false and misleading in any particular,"* to *"contain a summary of the essential scientific information needed for the safe and effective use of the drug,"* and prohibits *"implied claims or suggestions of drug use if there is inadequate evidence of safety or a lack of substantial evidence of effectiveness."*

73. The FDA has interpreted oral communications as falling under the umbrella of "labeling."

74. Section 99.101 et seq. lays out the stringent requirements that must be met by the manufacturer before it may disseminate any materials on unapproved or new uses of marketed drugs. This material must be in the form of an unabridged reprint or copy of a published, peer reviewed article that is considered *"scientifically sound"* by experts qualified to evaluate the safety or effectiveness of the drug involved. See 21 C.F.R. 99.101(a)(2). The FDA does not consider abstracts of publications to be *"scientifically sound."* 21 C.F.R. 99.101(b). Unabridged reprints or copies of articles shall not be disseminated with any information that is promotional in nature. 21 C.F.R. 99.101(b)(2).

75. Furthermore, the manufacturer must not disseminate materials that are "false and misleading," such as those that only present favorable information when unfavorable publications exist, exclude mandatory information about the safety and efficacy of the drug use, or present conclusions that "clearly cannot be supported by the results of the study." 21 C.F.R. 99.101(a)(4).

76. Additionally, off-label information may be disseminated only in response to an *"unsolicited request from a healthcare practitioner."* 21 U.S.C. § 360aaa-6. In any other circumstance, a manufacturer may disseminate information concerning off-label use only after it has submitted an application to the FDA seeking approval of the drug for the off-label use, has provided the materials to the FDA prior to dissemination; and the materials themselves are submitted in unabridged form and are neither false or misleading. 21 U.S.C. §§ 360aaa(b) & ©; 360aaa-1.

77. The FDA does not generally regulate the exchange of scientific information, but when such information is provided by or on behalf of a drug company regarding one of the company's products, the information may be subject to the labeling and advertising provisions of the law and regulations. For example, while information provided at continuing medical education programs - such as medical conferences and professional gatherings intended to enhance physicians' knowledge and enable them to meet certain practice requirements generally is not subject to FDA regulation, it will be if the program has been funded and substantially influenced by a drug company.

78. In sum, the off label regulatory regime protects patients and consumers by ensuring that drug companies do not promote drugs for uses other than those found to be safe and effective by an independent, scientific government body -- the FDA. The prohibition on unsubstantiated comparative claims protects patients and consumers by ensuring that the prescription and use of approved drugs is not based on misleading marketing tactics.

3. The FDA Has Limited Ability To Regulate Drug Maker Marketing and Promotion.

79. The FDA's Division of Drug Marketing, Advertising and Communications ("DDMAC") is charged with overseeing the marketing and promotion of approved drugs to ensure that advertisements are not false or misleading, provide a fair balance between the benefits and risks of the drug, and do not include off label uses. *See Statement by Janet Woodcock, M.D. (Director Center for Drug Evaluation and Research, FDA) Before the Senate Special Committee on Aging (July 22, 2003).*

80. DDMAC's effectiveness in regulating off label promotion is limited. In 2003, the entire staff consisted of forty members, with twenty-five reviewers responsible for reviewing all drug advertisements and promotional materials. Moreover, drug materials do not have to be pre approved. FDA review of promotional materials occurs, if at all, only after the materials already have appeared in public. *See Woodcock Statement, supra.* Upon finding a violation, DDMAC generally requests, but does not require, the company to stop using the

promotional materials. *Id.* Sponsors occasionally are required to publicly correct product mis-impressions created by false, misleading, or unbalanced materials. *Id.*

81. Once a drug has been approved, the FDA's statutory authority is limited to requesting label changes, negotiating restrictions on distribution with the manufacturer, and petitioning for the withdrawal of the drug from the marketplace. Title 21 of the Code of Federal Regulations requires that "as soon as there is reasonable evidence of' a serious hazard with a drug," the "Warnings" section of the label should be revised to reflect this hazard.

82. The FDA's ineffectiveness in policing off-label promotion was confirmed in a July 28, 2008 U.S. General Accountability Office Report, which found that the FDA took an average of seven (7) months to issue letters in response to off-label promotions. *See Drugs: FDA's Oversight of the Promotion of Drugs for Off-Label Uses (GAO 08-835), http:l/www.gao.gov/new.items/d08835.pdf.* Among the Report's findings: (i) FDA does not have separate oversight activities to specifically capture off-label promotion; (ii) FDA is unable to review all promotional submissions because of the volume of materials it receives and prioritizes its reviews in order to examine those with the greatest potential impact on human health; (iii) FDA is hampered by the lack of a system that consistently tracks the receipt and review of submitted materials; (iv) FDA conducts limited monitoring and surveillance to identify violations that would not be identified through its review of submitted material-for instance, discussions between doctors and sales representatives; (v) during calendar years 2003 through 2007, FDA issued 42 regulatory letters in

response to off-label promotions requesting drug companies to stop dissemination of violative promotions.

B. The Orphan Drug Program

83. The Orphan Drug Act ("ODA") was enacted in 1983, and it provides various incentives for pharmaceutical companies to develop drugs for the treatment of rare diseases and conditions, defined by the ODA to include *"any disease or condition which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug."* 21 U.S.C. § 360bb(a)(2); 21 C.F.R. § 316.20(b)(8). These drugs are referred to as "orphan drugs," and incentives for orphan drug development include (i) tax credits of up to 50% for qualified clinical research expenses, see 26 U.S.C. § 45c; 26 C.F.R. § 1.28-1; (ii) a seven-year period of marketing exclusivity to the first sponsor who obtains marketing approval for a designated orphan drug, whether or not the drug is patentable, see 21 U.S.C. § 360cc; 21 C.F.R. § 316.31; and (iii) eligibility for research grants, see 21 U.S.C. § 360ee.

84. The orphan drug development program is administered by the FDA's Office of Orphan Products Development ("OOPD"). In order for a sponsor to obtain the orphan designation for a drug or biological product, an application must be submitted to the OOPD. *See 21 C.F.R. §§ 316.20 & 316.21.* The approval of an application is based upon the information submitted by the sponsor, and the

designations are indication-specific. *See 21 C.F.R. § 316.20(b)(3).* The approval of a drug for orphan drug status does not alter the standard regulatory requirements and procedures for obtaining marketing approval; however, historically, the approval time for orphan products as a group has been considerably shorter than the approval time for other drugs.

85. The tax credit provisions of the ODA are administered by the Internal Revenue Service. *26 C.F.R. § 1.28-1.* By reducing the costs to develop drugs for small patient populations, the credit allows companies to develop products that would otherwise be commercially unfeasible. The Orphan Drug Tax Credit applies to qualified clinical trial expenses that are incurred after the FDA has designated the drug as an "orphan."

86. The seven-year period of marketing exclusivity that is provided to orphan drugs is limited to the indication for which the orphan designation was approved. *See 21 C.F.R. §316.31.* By precluding competition, this period of exclusivity provides a powerful financial incentive to an orphan drug's sponsor. The FDA funds the development of orphan products through the "Orphan Products Grants Program," which is administered by the OOPD and provides funding for clinical research in rare diseases.

C. Prescription Drug Payments Under Federal Healthcare and Other Programs

87. Whether an FDA-approved drug is approved for a particular indication (i.e., use) determines whether a prescription for that use may be reimbursed under Medicaid and other federal healthcare programs.

1. The Medicare Program

88. The Medicare Prescription Drug Improvement and Modernization Act of 2003 added prescription drug benefits to the Medicare program. Medicare serves approximately 43 million elderly and disabled Americans.

89. Federal statutes and regulations restrict the drugs and drug uses that the Federal Government will pay for through its funding of the Medicare program. Federal reimbursement for prescription drugs under the Medicare Prescription Drug benefit is limited to "covered outpatient drugs."

90. Covered outpatient drugs are drugs that are used for a "medically accepted indication." *42 U.S.C. § 1396x-8(k)(2)-(3).* A medically accepted indication, in turn, is a use that is listed in the labeling approved by the FDA, or that is included in one of three approved drug compendia: (i) the American Hospital Formulary Service Drug Information (AHFS-DI), (ii) the United Sates Pharmacopeia-Drug Information (or its successor publications); and (iii) the DRUGDEX Information System. *42 U.S.C. §§ 1396r-S(g)(1)(B)(i) and (k)(6).*